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EXAMINER	
NGUYEN, B	
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DATE MAILED: 05/20/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 10/20/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-77 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-77 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Part III DETAILED ACTION

Drawings

1. The informal drawings are not of sufficient quality to permit examination. Accordingly, new drawings are required in response to this Office action.

Specification

2. Page 22, Example 1 of the specification make reference to a Table 1, however, no such table is found in the application papers.

Temperature for the primary drying step and the moisture content after the primary drying step are recited in claims 14-18, however, these recitations are not disclosed in the specification.

Claim 26 recites a pressure of 0.01 to 30 Torr/mm Hg, which is not disclosed in the specification.

Claim 32 recites a temperature of 0°C to 80°C, which is not disclosed in the specification.

Claim 34 recites a moisture content of 0.1 to 12%, which is not disclosed in the specification.

Claim Rejections - 35 USC § 112

3. Claims 1-77 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the use of trehalose as the glass forming material. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification discloses a method of incorporating a biological substance into foamed glass matrices by adding trehalose and a solvent specific for the substance to be stored, the substance itself, and at least one other additive, the additive can be an inhibitor of the Maillard reaction or volatile salts or volatile organic solvents. The volatile salts and solvents are used to enhance foam formation. The additive can also be a foam stabilizing agent

The specification teaches evaporating the solvent and subjecting the resulting syrup to a temperature and pressure sufficient to boil the syrup causing bubbles to form, and removing the moisture thereby allowing the bubbles to form a glass-like material. The specification specifically teaches using trehalose, (alpha-D-Glucopyranoxyl-alpha-D-glucopyranoside), as the glass forming material. The specification also teaches chosing a solvent that is specific for the substance to be incorporated therein. The specification further teaches adjusting internal and external temperature and pressure so as to cause boiling of the syrup.

The specification does not teach modifying the carbohydrate either chemically or enzymatically.

The specification as disclosed is not enabled for all polyols or all natural, synthetic or modified carbohydrate as the glass forming material, as recited in the instant claims. It would require undue experimentation for one of ordinary skill in

the art to determine if all polyols or all carbohydrates show similar stability values when used as a glass forming material. Furthermore, it has been demonstrated in the prior art that not all sugars are appropriate for use as glass forming material. In Trehalose Drying: A Novel Replacement for Freeze-Drying, 1991, pp. 47-53, Roser stated that reducing sugars should be avoided. Roser further stated in Table 1 of the same publication, that tests on reducing and non-reducing sugar, with the exception of trehalose, show negative results for stability. In this publication, Roser also stated that any buffers used together with trehalose and the substance to be dried must be specific for the substance inorder for the substance to retain it's full activity when reconstituted. Roser also show in a 1993 publication, A sweeter way to fresher food, that reducing sugars such as lactose and maltose do not confer the same stability as trehalose. Neither do disaccharide, sucrose, sugar alcohols, dextran as well as monosaccharide and monosaccharide alcohols.

4. Claims 1-77 are rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-77 refer to temperatures and pressures and further recite values for these temperature and pressure, however, it is unclear whether these values are external pressure or external temperature values as is disclosed in the specification.

Claim 1 is vague and indefinite with respect to the recitation of "evaporating bulk solvent" and "temperature sufficient to cause boiling". It is unclear how much would define "bulk" or what would be "sufficient".

Claim 5 is vague and indefinite because it is not clear as to what on the carbohydrate has been modified.

Claim 6, 43, 55 and 58 are vague and indefinite with respect to the use of improper Markush language. The members of the Markush group are not clearly set forth. A proper Markush-type claim cannot have double inclusion of members. Further, a proper Markush-type claim must also use "and" before the last member of the group to close off the Markush group. In claim 6, sugar alcohol is being recited twice. In claim 43, alcohols, ethers and oils are all liquid hydrocarbons. The recitation of "liquid hydrocarbons" should be removed. In claim 55, the members are all organic. The recitation of "organics" should be removed. In addition, there are several double inclusion of members. Claim 58 also have double inclusion of members.

Claim 8 is vague and indefinite with respect to the recitation of "the solvent". It is unclear that this solvent is specific for the glass forming material.

Claim 9 is vague and indefinite with respect to the recitation of "biologically acceptable buffers". It is unclear what would define "biologically acceptable".

Claims 14, 19 and 30 are vague and indefinite with respect to the recitation of "ambient temperature". This term lacks proper definition.

Claim 18 is vague and indefinite with respect to the recitation of "conditions sufficient to remove". It is unclear what would define "sufficient".

Claim 47 is vague and indefinite with respect to the recitation of "amphipathic molecule". It is unclear what this molecule is.

Claim 50 is vague and indefinite with respect to the recitation of "bioactive substance". It is unclear what this term means or how it is related to the previously recited reagents.

Claims 52 and 68 are vague and indefinite with respect to the recitation of "therapeutically effective amount". It is unclear what this term means.

Claim 53 is vague and indefinite with respect to the recitation of "biological modifiers". It is unclear what these are.

Claim 59 and 61 are vague and indefinite with respect to the recitation of "a solvent". It is unclear that this solvent is specific for the substance to be reconstituted. Claim 61 is also vague and indefinite with respect to the recitation of "biologically acceptable buffer". It is unclear what this means.

Claim 60 is vague and indefinite with respect to the recitation of "therapeutically effective concentration". It is unclear what this means.

Claim 62 is vague and indefinite with respect to the recitation of "solvent" in lines 6 and 8. It is unclear that these solvent are specific for the glass forming material and the substance. Claim 62 is also vague and indefinite with respect to the recitation of "bulk solvent" and "sufficient to cause boiling". It is unclear what these terms mean.

Claims 63-64 and 66-67 are vague and indefinite with respect to the recitation of "solvent". It is unclear whether this solvent is specific for the glass forming material or specific for the substance.

Claim 65 is vague and indefinite with respect to the recitation of "solvent", "bulk solvent" and "sufficient to cause boiling". It is unclear whether the solvent is specific for the glass forming material or for the substance. The use of "bulk solvent" and "sufficient to cause boiling" are also unclear.

Claim 68 is vague and indefinite with respect to the recitation of "suitable solvent". It is unclear what this means. The abbreviation "FRG" should be clearly spelled out.

Claim 70 is vague and indefinite with respect to the recitation of "suitable solvent". It is unclear that this solvent is specific for the substance.

Claim 73-77 are vague and indefinite with respect to the recitation of "obtainable". It is unclear as to whether the composition can be obtained.

5. Claims 24 and 25 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 24 and 25 recite exposing the syrup to a temperature and pressure so as to cause boiling of the syrup and thereby forming bubbled glass. This does not further limits claim 1 from which claims 24 and 25 depend.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 6, 8, 9, 13-18, 24, 30-36, 40, 41, 49, 52-55, 62, 63, 76 and 77 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chivers (U.S. Patent No. 3,557,717).

Chivers teaches a method for making fine candy floss filaments from a molten liquid solution or syrup containing at least sugar and water (column 1, lines 2-5). Candy floss is a form of hard candy comprised of sugar in a noncrystalline, amorphous stated (column 4, lines 19-22). Chivers teaches mixing 85%-90% sucrose, 10%-15% water and a flavoring or coloring

ingredients, heating the solution to form a molten syrup, thereafter, boiling the syrup and removing the moisture so that the final content of the moisture is reduced to less than 1.5 percent (column 1, lines 48-54). Chivers teaches boiling the syrup at atmospheric pressure and high temperature ranging from 190°F to 300°F or even higher if desired (column 3, lines 35-75). Chivers also teaches adding butter to make caramel-flavored candy floss (column 5, line 30), molasses, salt and sodium bicarbonate (column 4, lines 37-40). These substances are added in a amount deemed appropriate for flavor and color.

8. Claims 71 and 72 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Wettlaufer et al (U.S. Patent No. 5,290,765).

Wettlaufer teaches a glassy, amorphous solid stated having enzymes or cells embedded therein (column 2, lines 40-54 and column 6, lines 18-30).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

> Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

10. Claims 10-12, 19-23, 25, 26-29, 42-47, 50, 52, 53, 57, 59-61, 64-69, 70 and 73-75 are rejected under 35 U.S.C. § 103 as being unpatentable over Chivers in view of Black (U.S. Patent No. 3,619,294), Samuels et al (U.S. Patent No. 5,422,384) and Wettlaufer (U.S. Patent No. 5,290,765).

See discussion of Chivers above. Chivers differs from the instant invention in failing to teach the use of volatile organic solvent, or varying the pressure to cause boiling of the syrup or boiling the syrup so that a glass-like substance is formed from the molten mixture. Chivers also did not teach adding medicinal agents to the solution nor reconstituting the final product in appropriate solvents.

Black teaches a method of combining sugar, organic and inorganic solvents and various additives to produce powdered-drinks or tablets. Black teaches the use of sugars such as sucrose, fructose, maltose, and lactose and a combination of organic or inorganic solvent (column 3, lines 59-60 and column 4, lines 1-8), evaporating the solvent to reduce the moisture content and when desired, reconstituting the final product with a suitable solvent. Black teaches the addition of volatile oils

and guar gum as a coating material (column 6, lines 52 and 75). Black also teaches the addition of medicines, vaccine and other fruit or liquor flavor such that when reconstituted can be used as drinks. Black also teaches that when a medicinal agent or vaccine is incorporated in the final product, it is present in a therapeutically appropriate amount (column 10, lines 7-10).

Samuels teaches a method of making a glass/polymer composite by mixing a glass making material with an appropriate solvent. Heating the solution to evaporate the solvent leaving a molecular mixture, gel or the like. And heating the mixture to produce a glass/polymer composite (column 4, lines 6-12). Samuels teaches a mixture of both inorganic and organic solvent such as alcohols and ethers (column 4, lines 14-20 and column 5, lines 38-40). Samuels also teaches elevating the temperature and pressure as desired. The temperature can be elevated to 40°C or 100°C (column 5, lines 11-14).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to adjust the temperature and pressure, as taught by Samuels, in the method of Chivers to optimize the heating and evaporation procedure because Samuels shows it to be conventional in the art.

It would have been obvious to one of ordinary skill in art at the time the invention was made to use a mixture of organic and inorganic solvent such as taught by Black, because organic

solvent aid in the dispersion of the additives or modying agent (Black, column 4, lines 1-5).

It would have been obvious to one of ordinary skill in the art that the fine floss filament of Chivers is in a noncrystalline amorphous state, which, by deffinition, is a glossy glass-like material in the form of fine filament. This form of glass-like product is obtained when most of the moisture is removed from the mixture. It is well know in the art that the ability to form a glassy solid state is indicative of soluble sugar under appropriate conditions (Wettlaufer, U.S. Patent No. 5,290,765).

In addition, it would have been obvious to one of ordinary skill in the art at the time the invention was made that various additives may be included in the mixture (Chivers, column 3, lines 5-10). One of ordinary skill would have had a reasonable expectation of success in using the medicinal agents and vaccine of Black in the method of Chivers because Black shows it to be well known and conventional in the art.

11. Claim 7 is rejected under 35 U.S.C. § 103 as being unpatentable over Chivers in view of Roser (GB 2,206,273).

See discussion of Chivers above. Chivers differs from the instant invention in failing to teach the use of trehalose as the sugar.

Roser teaches a similar invention whereby trehalose is used to preserve proteinaceous material. Roser teaches trehalose mixed with proteinaceous foodstuffs and heated to high temperatures, 40°C to 80°C, or 175°C to 205°C, or 85°C or 98°C (page 6). Roser also teaches that the resultant product can be reconstitute in appropriate solvent.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to use the trehalose, as taught by Roser, in the method of Chivers because Roser shows that trehalose is more efficient than other sugars and does not rendered the product too sweet (page 4).

Allowable Subject Matter

12. Claims 36-39, 48, 51, 56, and 58 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. The following is an Examiner's statement of reasons for the indication of allowable subject matter:

Claims 36-39, 48, 51, 56 and 58 are allowable over the prior art of record because the use of trehalose as the glass-matrix forming material along with volatile salt additives and Maillard reaction inhibitors to preserve cells, enzymes, and vaccine etc. at high temperature and in long term storage is novel.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

3,632,357 Childs
3,655,422 Schwer et al.
4,127,502 LiMutti et al.
4,158,544 Louderback
4,327,076 Puglia et al.
4,327,077 Puglia et al.
4,588,744 McHugh
4,701,417 Portenhauser et al.
4,762,857 Bollin, Jr. et al.
4,865,871 Livesey et al.
4,883,762 Hoskins
5,348,852 Bonderman
WO 92/02133 Bonderman
EP 0415567 Roser
WO 87/00196 Roser
WO 95/33488 Roser

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Number is (703) 308-4065.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy Nguyen whose telephone number is (703) 308-4243. In the event that the Examiner is unavailable, please contact the Supervisor Patent Examiner, James Housel whose telephone number is (703) 308-4027.

Any inquiry of a general nature or relating to the status of application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

BTN
May 13, 1996

Christopher L. Chin

CHRISTOPHER L. CHIN
PATENT EXAMINER
GROUP 1800